limitations of the base claim and any intervening claims.

At page 2 of Paper No. 5, the Examiner has rejected claims 15-19 under 35 U.S.C. § 101, because of the claims' recitation of a "use." Claims 15-19 have been cancelled, without prejudice. Accordingly, the Examiner's rejection is no longer applicable. Its reconsideration and withdrawal are respectfully requested.

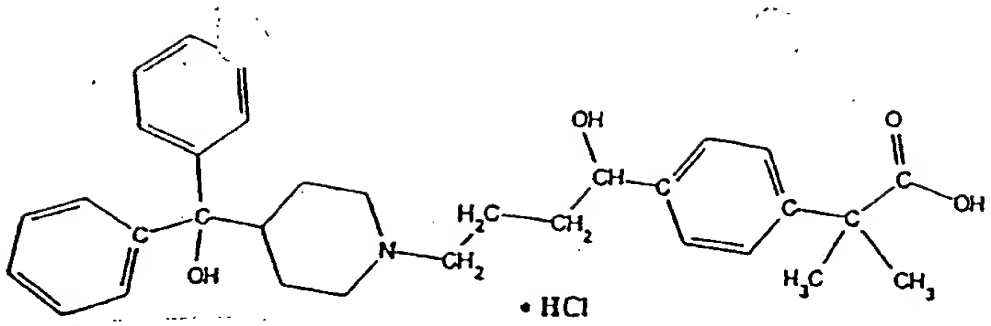
Applicants Invention.

The applicants respectfully disagree with the Examiner's characterization of the invention, as set forth on page 2 of Paper No. 5. In particular, the Examiner asserts that the "route of administration is not critical in a composition claim" and "what the excipient does is not critical in a composition claim." In the present situation, this statement is not correct. The function of an element of a claim is to be considered for purposes of patentability if such function impacts a structural limitation to the element. The present invention is directed to, *inter alia*, a pharmaceutical excipient that increases the solubility of fexofenadine and a composition which is in a form adapted for administration to the nose or eye. Each of these functional requirements implicates a structural, physical aspect of the compound or substance which it modifies. Thus, each should be given consideration when considering the patentability of the claims.

Rejection Under 35 U.S.C. § 102(b) Based Upon U.S. Patent No. 5,691,370.

The Examiner has rejected claims 1-4, 9-14, 20 and 22 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,691,370 of Cupps *et al.* ("Cupps"). As basis for this rejection, the Examiner alleges that Cupps discloses a pharmaceutical composition comprising terfenadine or terfenadine carboxylate, in combination with carriers and suspending agents. The applicants traverse this rejection for the reasons set forth below.

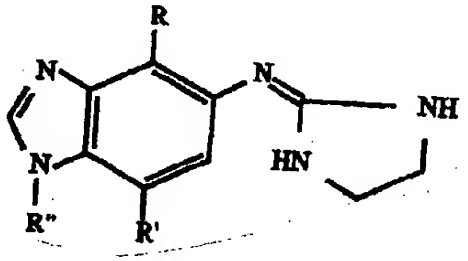
In order to anticipate a claim, the reference must teach each element of the claim. Cupps fails this test. The invention is a composition comprising fexofenadine or a pharmaceutically acceptable salt thereof and an excipient which increases the solubility of the fexofenadine or salt of fexofenadine in water. Fexofenadine (or its salt) is represented by the structure shown below:



Fexofenadine hydrochloride

The invention also encompasses a method of treating a patient using the claimed fexofenadine-containing composition.

In contrast, Cupps does not disclose a composition comprising fexofenadine or a pharmaceutically acceptable salt. The composition of Cupps contains a compound having the structure:



where R is an unsubstituted alkanyl or alkenyl having from about 1 to about 3 carbon atoms; R′ is selected from hydrogen, unsubstituted alkanyl or alkenyl having from about 1 about 3 carbon atoms, unsubstituted alkylthio or alkoxy having from about 1 to about 3 carbon atoms, hydroxy thiol, cyano, and halo. R′ is selected from a hydrogenation, methyl group, ethyl group, and i-propyl group. *See*, Col. 3 of Cupps.

As can be seen by comparison of the two structures, Cupps does not disclose a composition containing fexofenadine or a salt of fexofenadine. Because Cupps does not teach the active agent fexofenadine or its salts, Cupps fails to teach each element of the claimed invention. Consequently, Cupps does not anticipate it under § 102(b).

For the reasons set forth above, it is respectfully requested that the Examiner reconsider and withdraw her § 102(b) rejection based upon Cupps.

Rejection Under 35 U.S.C. § 102(e) Based Upon U.S. Patent Nos. 6,120,803 and 6,027,046, Taken Individually.

At page 3 of Paper No. 5, the Examiner has rejected claims 1-3, 14, and 20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,120,803 of Wong *et al.* ("Wong").

As basis for this rejection, the Examiner asserts that Wong discloses a composition comprising fexofenadine, surfactants, carriers, and excipients that "meets the limitations of the claims."

At page 4 of Paper No. 5, the Examiner has rejected claims 1-3, 12-14, and 20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,027,746 of Lech ("Lech"). As basis for the rejection, the Examiner asserts that Lech discloses a pharmaceutical composition comprising fexofenadine, excipients, and poloaxamer 407, which "meets the limitations of the claims."

The applicants respectfully traverse the rejections based upon Wong and Lech, each taken individually.

Wong discloses an active agent dosage form adapted for retention in the stomach and therefore useful in the prolonged delivery of an active agent formulation to a fluid environment. The Wong active agent dosage form is solid capsule having a diameter of 7mm to greater that 13 mm. The capsule is made of a polymer matrix that swells upon contact with the water.

A portion of the swellable polymer matrix of Wong is surrounded by a band of insoluble material that prevents the protected portion of the polymer matrix from contact with fluid and therefore from swelling. Wong teaches that the insoluble band permits the capsule to withstand the muscular contractions of the stomach and thereby remain in the stomach until all of the active agent has been released from the swellable polymer matrix. Wong discloses a lengthy list of active agents that may be dispersed in the swellable polymer matrix. See col. 18, line 1 to col. 20, line 2. Among these is fexofenadine. Additionally, Wong teaches that the dosage form may include non-polymeric water-soluble excipients. Col. 6, lines 13-31.

Lech teaches a pharmaceutical delivery system comprising a chewy, soft gelatin capsule within which a drug adsorbate is dispersed in a solid or liquid fill material. Lech teaches a list of suitable drugs for use in the chewy capsules, including fexofenadine. The drug incorporated into the chewy capsule is adsorbed onto flake-like particles of an adsorbate, such as magnesium trisilicate or silicate dioxide. Because the drug is adsorbed to the flake-like adsorbate materials it is thereby prevented from dissolving into the liquid or solid excipient. Such drug adsorbate complex is critical to Lech; because the active agent is prevented from dissolving, the patient does not taste it when the capsule is administered orally. Suitable aqueous-based fill materials for use in the capsule, include water, combined with a second

excipient which, according to Lech, may be sorbitol, glycerine, corn syrup, sugar, alcohols, and mixed with such substances. The composition of Lech is specifically adapted for oral administration.

Neither Wong nor Lech, each taken individually, teaches each element of the invention. First, neither Wong nor Lech teaches a pharmaceutical excipient that increases the solubility of fexofenadine or the salt of fexofenadine. No disclosure of such excipients is given in Wong at Col. 6 (where excipients are disclosed), nor is there any indication that it would be desirable to select excipients that act to increase the solubility of fexofenadine or its salts.

Similarly, Lech teaches a drug adsorbate (i.e., a flake-like compositions to which the selected drug is "fixed") that is suspended in a fill material, which may be solid or liquid. The fill material is clearly not one that increases the solubility of fexofenadine or its salts; to the contrary, it must be a material in which fexofenadine and its salts are insoluble, for, if the active agent was to be dissolved from the flake to which it is adsorbed the taste-masking function of the delivery system would be defeated.

In contrast, the composition of the present invention comprises an excipient that increases the solubility of fexofenadine or its salts in water. Similarly, the method discloses a method of treatment which involves administration of the same composition.

Second, neither Wong nor Lech discloses a composition adapted for administration to the eye or nose. The Wong capsule in relatively large in size, and requires immersion in fluid

Thus, in view of the foregoing, it is respectfully submitted that neither Wong nor Lech teaches each element of the claimed invention, and therefore neither is anticipatory of the invention. Reconsideration and withdrawal of the § 102(e) rejections based upon Wong and Lech, taken individually, are respectfully requested.

Rejection Under 35 U.S.C. § 102(e) Based Upon U.S. Patent No. 6,117,452.

The Examiner has also rejected claims 1-4, 12-14, and 20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,117,452 of Ahlgren *et al.* ("Ahlgren"). As basis for this rejection, the Examiner asserts that Ahlgren discloses a composition comprising fexofenadine, excipients, and surfactants such as poloxamers, tweens, and spans. The Examiner contends that Ahlgren specifically states that transdermal, buccal, and nasal dosages are

contemplated. The applicants respectfully traverse this rejection.

Ahlgren relates to the preparation of thermoformed particulates of active agents. The compositions to be processed contain one or more active agents, a combination of processing aids, such as glyceryl monostearate, and polyethylene glyceryl palmitostearate, and one or more optional emulsifiers and/or surfactants. Ahlgren teaches fexofenadine as an active agent that one could choose to use as an active agent in the thermoformed particles of Ahlgren. In Col. 6, lines 28-30, Ahlgren indicates that the thermoformed compositions are preferred to be orally ingestible units, such as tablets, pills, capsules, troches, and liquid suspensions. In the same passage, Ahlgren also states that transdermal, buccal, and nasal products are contemplated within the scope of the invention. However, all of the specific examples set forth in Ahlgren are for the manufacture of orally ingestible units; no specific disclosures of dosage units suitable for nasal administration are disclosed. Accordingly, Ahlgren does not specifically disclose a composition that is adapted for administration to the eye or nose.

In contrast to Ahlgren, the present invention is directed to compositions adapted for administration to the eyes or nose.

Additionally, the Ahlgren composition does not specifically teach an excipient which increases the solubility of fexofenadine or a salt of fexofenadine in water as is claimed in the present invention. To the contrary, Ahlgren requires use of water insoluble excipients, such as glyceryl monostearate, which, by virtue of their water insolubility are structurally unable to enhance the solubility of fexofenadine in water, and may, in some case, reduce such solubility.

Accordingly, for the reasons set forth above, it is respectfully submitted that Ahlgren does not teach or suggest each element of the claimed invention. Therefore, it does not anticipate the invention as claimed and reconsideration and withdrawal of the rejection based on Ahlgren is respectfully requested.

Rejection Under 35 U.S.C. § 102(a) Based Upon the Physician's Desk Reference (pp.1189-1190)(1998).

The Examiner has rejected claims 1-3, 9-11, 14, 20, and 22 under 35 U.S.C. § 102(a) based upon the teachings of the Physician's Desk Reference, pages 1189-1190 (1998) ("PDR"). As basis for this rejection, the Examiner asserts that the PDR discloses a capsule dosage form of fexofenadine (Allegra™) which comprises excipients and other additives such as

iron oxide, gelatin, silicon dioxide, titanium dioxide, and sodium lauryl sulfate. The applicants traverse the rejection for the reasons set forth below.

The PDR discloses capsules containing 60 mg of fexofenadine hydrochloride and specific excipients. The disclosed excipients are croscamellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. The outer shell of the capsule contains iron oxide gelatin, silicon dioxide, titanium dioxide and sodium lauryle sulfate. The active agent is not dissolved in the outer shell compounds.

The composition disclosed in the PDR does not teach each element of the claimed invention. First, the composition of the PDR is a solid dosage form. There is no mention of any other type of dosage form, nor is there any articulation that such dosage form is adapted for administration to the eye or nose. Further, none of the excipients used in the capsules of the PDR act to increase the solubility of fexofenadine in water. In contrast, the present invention requires that the excipients utilized in the composition increase the solubility of fexofenadine in water.

Accordingly, for the reasons set forth above the PDR does not teach or suggest each element of the claimed invention and is not anticipatory of it. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw her rejection based upon the PDR.

CONCLUSION

In view of the foregoing, it is submitted that claims 1-14 and 20-22 are fully distinguished the cited prior art of record. Accordingly, the applicants respectfully request reconsideration and withdrawal of the Examiner's rejections.

Respectfully submitted,

LISBETH ILLUM *et al.*

11/29/01
(Date)

By: Kristyne Bullock for Reg No. 35837
KRISTYNE A. BULLOCK
Registration No. 42,371

AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P.
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103
Telephone: (215) 965-1200
Direct Dial: (215) 965-1348
Facsimile: (215) 965-1210
E-Mail: kbullock@akingump.com

WWS/KAB/vj

Enclosures: *Marked-Up Version of Specification*
Marked-Up Version of Claims

Marked-Up Version of the Specification

U.S. Patent Application No. 09/834,312

Shown below are the changes to replacement paragraph 0001 of the specification marked up to show the changes made. Please note that deletions are indicated by brackets and insertions are indicated by underlining.

[0001] This application is a continuation of International Application No. PCT/GB99/03396, filed October 12, 1999, and published in the English language on April 20, 2001, the disclosure of which is incorporated herein by reference.

Marked-Up Version of Claims 2, 4-7, 9-13, and 20-22

U.S. Patent Application No. 09/834,312

Shown below are the amended claims 2, 4-7, 9-13, and 20-22, marked up to show the changes made. Please note that deletions are indicated by brackets and insertions are indicated by underlining.

2. (Amended) A composition as claimed in [Claim] claim 1 for use in medicine.

4. (Amended) A composition as claimed in [Claim] claim 3, wherein the solvent is propylene glycol or glycofurol (tetraglycol).

5. (Amended) A composition as claimed in [Claims] claim 1, wherein the pharmaceutical excipient is a material which is able to complex with the fexofenadine or pharmaceutically acceptable salt thereof.

6. (Amended) A composition as claimed in [Claims] claim 1, wherein the pharmaceutical excipient is a cyclodextrin.

7. (Amended) A composition as claimed in [Claim] claim 6, wherein the cyclodextrin is hydroxypropyl-β-cyclodextrin.

9. (Amended) A composition as claimed in [Claims] claim 1, which further comprises a gelling agent or bioadhesive material.

10. (Amended) A composition as claimed in [Claim] claim 9, wherein the gelling agent or bioadhesive material is a polysaccharide.

11. (Amended) A composition as claimed in [Claim] claim 10, wherein the gelling agent or bioadhesive material is selected from the group consisting of pectin, alginate, starch, gellan and chitosan.

12. (Amended) A composition as claimed in [Claim] claim 9, wherein the gelling agent is a block co-polymer.

13. (Amended) A composition as claimed in [Claim] claim 12, wherein the block co-polymer is a poloxamer.

20. (Amended) A method of treating a patient in need of treatment with fexofenadine or a pharmaceutically acceptable salt thereof which comprises administering an effective amount of a composition according to [Claim] claim 1 to a patient in need of such treatment.

21. (Amended) A method of treating rhinitis which comprises administering an effective amount of a composition according to [Claim] claim 1, to a patient in need of such treatment.

22. (Amended) A method of treating a patient with a controlled release dose of fexofenadine or a pharmaceutically acceptable salt thereof which comprises administering an effective amount of a composition according to [Claim] claim 9, to a patient in need of such treatment.